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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/758,672	01/15/2004	Hui-Quan Han	01017/35966B	1279

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EXAMINER	
SLOBODYANSKY, ELIZABETH	

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 11/10/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/758,672	HAN ET AL.	
	Examiner	Art Unit	
	Elizabeth Slobodyansky, PhD	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 September 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *9,12-14,16-18,40-45,49,50 and 58* is/are pending in the application.

4a) Of the above claim(s) *9,12 and 58* is/are withdrawn from consideration.

5)☒ Claim(s) *13* is/are allowed.

6)☒ Claim(s) *14,16-18,40-45,49 and 50* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *15 January 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *4/30/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 9, 12-14, 16-18, 40-45, 49, 50 and 58 are pending.

Election/Restrictions

Applicant's election with traverse of Group IV, claims 13, 14, 16-18, 40-45, 49 and 50, in the reply filed on September 7, 2005 (page 1) is acknowledged.

The traversal is on the ground(s) that "In this response, the applicants interpret the examiner's assertion as identifying the subject matters of claim Groups I, III, and IV as dependent yet distinct subject matters, and not as independent subject matters. Additionally, the above quote from the Office Action asserts that the molecules are divergent and have different structures, functions and utilities. The applicants request clarification of the meaning of "divergent" molecules, and further request the provision in the M.P.E.P. that provides a basis for restricting assertedly distinct inventions on the basis of different structures, functions and utilities" (Response, page 1 through page 2, 1st paragraph). The meaning of "divergent" molecules is understood as "differing" from each other. It is not necessary to provide the M.P.E.P. quotation for each particular example of distinct inventions. With regard to chemical compound such as polypeptides and polynucleotides the basis for distinctiveness lies in the different structures of these two classes of compounds. Different structures result in different functions, which, in turn, result in different utilities. Such differences are sufficient to provide the basis for the restriction. Each of these compounds has utility by itself (see MPEP 816, for example). Applicants further argue the restriction between product and process claims.

They argue the restriction between Group I and Group IV (pages 2-5). Applicants argue "The examiner did not cite § 806.05(f) and did not establish the process of claim Group I was not an obvious process of making the polypeptide, did not establish that the process of claim Group I could be used to make other and different products and did not establish that the product polypeptide could be made by another and materially different process" (page 2). It is agreed that claim 9 and claim 13 are related as process of making and product made. The inventions are distinct if either or both of the following can be shown: (1) that the process as claimed can be used to make other and materially different product or (2) that the product as claimed can be made by another and materially different process (MPEP § 806.05(f)). In the instant case the polypeptide can be purified from the human tissue using biochemical methods or can be synthesized chemically (specification, page 49). Furthermore, with regards to all and any of process claims, Applicants are reminded that "**Process claims that depend from or otherwise include all the limitations of the patentable product** will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier" (Office action mailed August 1, 2005, page 5).

The requirement is still deemed proper and is therefore made FINAL.

Claims 9, 12 and 58 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to nonelected Groups I-III and V, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on September 7, 2005.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 14, 16-18, 40, 41, 43-45, 49 and 50 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 14 recites (b) "an ortholog of SEQ ID NO:2" and (c) "an allelic or splice variant of either the amino acid sequence as set forth in SEQ ID NO:2, or at least one of (a)-(c)", i.e. allelic or splice variants of orthologs and derivatives of SEQ ID NO:2.

The art teaches the mouse ortholog of human ubiquitin ligase, huE3α (SEQ ID NO:2), (Kwon et al, PNAS, 1998, Vol. 95, pages 7898-7903, form PTO-1449 filed 4/30/04, reference C15) and rabbit, yeast and *C. elegans* orthologs (specification, page 2, lines27-32). The specification teaches only one allele within the scope of the genus, SEQ ID NO:2 encoded by SEQ ID NO:1. There is no description of the mutational sites that exist in nature, and there is no description of how the structure of SEQ ID NO;1 relates to the structure of other allelic or splice variants. The general knowledge in the art concerning allelic and splice variants does not provide any indication of how the structure of one allele is representative of unknown allelic and splice variants. The

common attributes of the genus are not described. One of skill in the art would conclude that applicant was not in possession of the claimed genus because a description of only one member of this genus is not representative of the variants of the genus and is insufficient to support the claim.

Claim 16 recites polypeptides having the amino acid sequence as set for the in SEQ ID NO:2 with at least one conservative or any substitution, insertion, deletion, truncation or the combination of the above. The number of said modifications is not limited negating, in effect, the reference to SEQ ID NO:2. Such recitation without the limitation on the number of the modifications fails to provide a sufficient description of the claimed genus of proteins as it merely describes the functional features of the genus without providing any definition of the structural features of the species within the genus.

The Court of Appeals for the Federal Circuit has recently held that a "written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as be structure, formula [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." University of California v. Eli Lilly and Co., 1997 U.S. App. LEXIS 18221, at *23, quoting Fiers v. Revel, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) (bracketed material in original). To fully describe a genus of genetic material, which is a chemical compound, applicants must (1) fully describe at least one species of the claimed genus sufficient to represent said genus whereby a skilled artisan, in view of the prior art, could predict the structure of other species encompassed by the claimed genus and (2) identify the common characteristics of the claimed molecules, e.g., structure, physical and/or chemical

characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or a combination of these".

In the instant case, the specification discloses human ubiquitin ligase, huE3α of SEQ ID NO:2 encoded by SEQ ID NO:1, *supra*. The specification fails to describe any other representative species by any identifying characteristics or properties other than having "an activity of the polypeptide of SEQ ID NO:2" and fails to provide any structure: function correlation present in all members of the claimed genus.

Therefore, the claims fail to provide an adequate written description of the genus of variant polypeptides of SEQ ID NO:2. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus.

Claims not specifically discussed above are rejected as dependent from the rejected base claim.

Claims 14, 16-18, 40-45, 49 and 50 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a polypeptide of SEQ ID NO:2, does not reasonably provide enablement for a polypeptide having an amino acid sequence at least 70, 80, 85, 90, 95% identical to SEQ ID NO:2 or having no known percent identity to SEQ ID NO:2 and retaining E3α ubiquitin ligase activity as well as a polypeptide having no defined activity or having E3α ubiquitin ligase activity that is encoded by a nucleotide sequence that hybridizes under highly stringent conditions to SEQ ID NO:1. The specification does not enable any person skilled in the art to which it

pertains, or with which it is most nearly connected, how to make and/or use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

The specification does not support the broad scope of the claims which encompass polypeptides E3α ubiquitin ligase activity and having an amino acid sequence at least 70, 80, 85, 90, 95% identical to SEQ ID NO:2, having no known percent identity to SEQ ID NO:2 or encoded by a nucleotide sequence that hybridizes under highly stringent conditions to SEQ ID NO:1 because the specification does **not** establish: (A) regions of the protein structure which may be modified without affecting E3α ubiquitin ligase activity; (B) the general tolerance of E3α ubiquitin ligase to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any residues in E3α ubiquitin ligase with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Furthermore, with regard to the naturally occurring proteins, while recombinant hybridization techniques are known, only highly homologous sequences can be

identified using a given sequence. The state of the art provides no reasonable expectation of success in obtaining a E3α ubiquitin ligase and having an unknown identity to SEQ ID NO:2 and the result of such screening is unpredictable.

Without sufficient guidance, beyond that provided, obtaining a polypeptide having an amino acid sequence at least 70, 80, 85, 90, 95% identical to SEQ ID NO:2 or having no known percent identity to SEQ ID NO:2 and retaining E3α ubiquitin ligase activity, a polypeptide having no defined activity and encoded by a nucleotide sequence that hybridizes under highly stringent conditions to SEQ ID NO:1, is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)).

Furthermore, claim 17 comprises polypeptides having E3α ubiquitin ligase activity and having no defined activity. Therefore, the breadth of these claims is much larger than the scope enabled by the specification. The specification does not teach how to use polypeptides having no known function. The state of the art does allow the predictability of the properties based on a given structure.

Without sufficient guidance, beyond that provided, one of ordinary skill in the art would not know how to use polypeptides with an undefined function. Therefore, the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)).

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 14, 16-18, 40-45, 49 and 50 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 14(a) recites "the mature amino acid sequence as set forth in SEQ ID NO;2 comprising a mature amino terminus at residue 1, optionally further comprising an amino terminal methionine". Claim 42 recites "the mature amino acid sequence as set forth in SEQ ID NO:2". The specification defines "mature huE3α polypeptide sequence" by non-limiting examples, including SEQ ID NO:2 (page 26, lines 16-21). Therefore, the metes and bounds of the term are not clearly defined. Furthermore, SEQ ID NO:2 contains methionine at position 1. Thus, it is unclear what is claimed as an optional sequence in claim 14(a).

Claims 14 and 16 recite "the polypeptide has an activity of the polypeptide set forth in SEQ ID NO:2". Such polypeptide can have various activities, including E3α activity, immunogenic activity, etc (specification, page 25, lines 24-32). Without defining the activity, it is impossible to know the metes and bounds of the claims.

Claim 17 recites "highly stringent conditions". Said conditions are defined by non-limiting examples, rendering the metes and bounds of the claim unascertainable (specification, pages 14-16). Claim 17 further recites "a nucleotide sequence complementary to any of (a)-(c)". The degree of complementarity is not defined,

rendering the claim unclear. Furthermore, SEQ ID NO:1 comprises both coding sequence and its complement. Therefore, reciting hybridizes to "SEQ ID NO:1" as opposed "the complement thereof" is sufficient.

Claim 44 is unclear because it is not clear which of the two polypeptides recited in base claim 43 is covalently modified with a water-soluble polymer. It is noted that the term "derivative" is defined by non-limiting examples rendering the metes and bounds thereof unascertainable (pages 24-25).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 14, 16-18 and 40-43 are rejected under 35 U.S.C. 102(b) as being anticipated by Kwon et al.

Kwon et al, *supra*, teach the mouse ortholog of human ubiquitin ligase (huE3α, SEQ ID NO:2) having the amino acid sequence consisting of 1757 amino acid residues that is 93.4% identical to SEQ ID NO:2. They teach the DNA encoding thereof that will hybridize to SEQ ID NO:1 under highly stringent conditions.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Elizabeth Slobodyansky, PhD whose telephone number is 571-272-0941. The examiner can normally be reached on M-F 10:00 - 6:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, PhD can be reached on 571-272-0928. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

E. Slobodyansky

Elizabeth Slobodyansky, PhD
Primary Examiner
Art Unit 1652

November 4, 2005